THE MANAGEMENT OF FRAGILITY FRACTURES OF THE HIP: A QUALITY ASSESSMENT PROJECT

By

NTAMBUE KAUTA

KTXNTA001

SUBMITTED TO THE UNIVERSITY OF CAPE TOWN

In fulfilment of the requirements for the degree

MASTER OF MEDICINE

ORTHOPAEDIC SURGERY (CHM7036W)

Faculty of Health Sciences

UNIVERSITY OF CAPE TOWN

University of Cape Town

Date of submission 14.08.2016

SUPERVISOR

DR SITHOMBO MAQUNGO

DEPARTMENT OF ORTHOPAEDIC SURGERY

UNIVERSITY OF CAPE TOWN

The copyright of this thesis vests in the author. No quotation from it or information derived from it is to be published without full acknowledgement of the source. The thesis is to be used for private study or non-commercial research purposes only.

Published by the University of Cape Town (UCT) in terms of the non-exclusive license granted to UCT by the author.

University of Cape Town

DECLARATION

I, Dr Ntambue Kauta, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

I empower the university to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

Signature: …NTAMBUE KAUTA…….

Date: …14/08/2016…….

ABSTRACT

Introduction

Fragility fractures of the hip (FFH) constitute the most serious complication of osteoporosis carrying a mortality rate of up to 20 – 30% in the first year after injury and are associated with post injury decay in patient's level of activity in more than 50% of the cases. It is also a predictor of future osteoporosis related fractures.

Surgical fixation of the hip fracture within 48 hours of admission, multimodal pain management, deep vein thrombo-prophylaxis, early physical therapy, appropriate assessment and management of osteoporosis and frailty in a multidisciplinary approach are the standard of care for FFH to keep the mortality and morbidity rate as low as possible and prevent future fragility fractures.

Aim

To assess the standard of care of FFH at our institution and determine areas of care which need more attention and improvement.

Methods

Retrospective review of clinical and radiographic records of all patients admitted at our level 1 trauma unit for fragility fracture of the hip from 1st January 2014 to 31st December 2014.

The waiting time from admission to surgical fixation of the hip fracture, pain control and thrombo-prophylaxis strategies, the rate of geriatric referrals and the extent of osteoporosis management were assessed.

Results

We admitted 113 fragility fractures of the hip from 1st January to 31st December 2014, 98 clinical records and 98 pelvis radiographs were included in the study. The other 15 clinical records were incomplete and were therefore excluded.

The average waiting time from admission to surgery was 49 hours (range 9 - 120). All patients received low dose morphine, paracetamol and tramadol for perioperative pain control. Low molecular weight heparin and compression stockings were prescribed for thrombo-prophylaxis in all patients.

Only 2 (2, 04%) patients had some osteoporosis investigations ordered and none of the patients were referred to the geriatric department, none of them were formally treated for osteoporosis.

Conclusion

While the waiting time from admission to surgery was largely within the recommended time frame, there were no signs of a multidisciplinary approach to the management of fragility fractures of the hip at our institution leaving osteoporosis and frailty largely untreated.

Key words: fragility fracture, geriatric hip fracture, hip fractures standard of care, osteoporosis, frailty care.

TABLE OF CONTENTS

PART A – RESEARCH PROTOCOL

I. Introduction
II. Methods
III. Relevance
IV. Report of findings
V. Budget and funding
VI. Ethical considerations
VII. References

PART B – LITERATURE REVIEW

I. Objectives of literature review
II. Search methodology
III. Introduction
IV. Aetiology of fragility fractures of the hip(FFH)
V. Osteoporosis overview
VI. Standard of care for FF
VII. References

PART C – MANUSCRIPT (PUBLICATION READY FORMAT)

PART D – APPENDICES

I. Acknowledgements

II. Ethic's approval

PART A - RESEARCH PROTOCOL

THE MANAGEMENT OF FRAGILITY FRACTURES OF THE HIP: A QUALITY ASSESSMENT PROJECT.

MMed student: Dr Ntambue Kauta

Supervisor: Dr Sithombo Maqungo

Co-investigators: Dr M Held, Dr S Dlamini, Dr S Kalula, Dr I Ross, Dr G Kalla

I. INTRODUCTION

Fragility fractures of the hip (FFH) are defined as fractures due to a low energy trauma such as falling from standing height as a result of a decrease in bone mass. These fractures are commonly seen in old age and are recognised as complications of osteoporosis in its various forms.[1] The incidence of FFH is expected to continue rising due to the ever increasing life expectancy seen across developed and emerging countries worldwide.

It is estimated that 1 in 3 postmenopausal women and 1 in 5 men over the age of 75 will suffer a FFH in their life time. The rising global prevalence of FFH is estimated to reach 2.6 million in 2025 and 6.3 million by year 2050.[2]

FFH constitutes the most serious complication of osteoporosis carrying a mortality rate of up to 20 – 24% in the first year after injury and is associated with post injury decline in patients' level of activity in more than 50% of the cases.[2,3]

The understanding that patients affected by FFH often present with a background of significant medical co-morbidities and frailty has led to the development of strict management guidelines with emphasis on a multidisciplinary approach to improve survival rate and clinical outcome after a FFH.

The American Academy of Orthopaedic Surgeons clinical practice guidelines stipulate that surgical fixation of the hip fracture within 48 hours of admission coupled with multimodal pain treatment, DVT prophylaxis, frailty care and osteoporosis management will ensure a positive clinical outcome. The pre-surgery waiting time should only be allowed for medical management of unstable or uncontrolled co-morbid conditions.[4]

Studies have shown a tendency to neglect the management of osteoporosis and frailty in patients who have been treated for FFH at various orthopaedic centres across the world with only 2% to 8 % of these patients being referred for osteoporosis treatment.[3, 5]

The purpose of our study is to evaluate the standard of management of fragility fractures of the hip at our institution by determining the waiting time from admission to surgical fixation of the fracture, the common mode of analgesia and DVT prophylaxis and management of osteoporosis and frailty.

II. METHODS

Retrospective review of clinical and radiographic records of all patients treated at our institution for fragility fractures of the hip from the 1st of January 2014 to 31st December 2014.

Patient's details were obtained from our admissions records and matched with details on our surgical database. We were able to retrieve their folders from our records department and their radiographs were available on our digital PACS (Picture archiving and communication system).

Folders were examined to determine the waiting time from admission to surgical fixation of the fracture, the common mode of analgesia and DVT prophylaxis, the rate of geriatric referrals and the extent of management of osteoporosis and frailty.

Inclusion criteria

- Hip fracture sustained from a fall from standing height or lower.
- Availability of patient's folder with clearly documented mechanism of injury, date and time of admission, date and time of surgery and x-rays

Exclusion criteria

- High energy hip fractures
- Pathological hip fractures due to malignant lesions or infection
- Incomplete records

Study measures

Patient's records were reviewed to determine the following measures:

- In hospital or postoperative out-patients investigations for osteoporosis (DEXA Scan, erythrocyte sedimentation rate(ESR), thyroid stimulating hormone(TSH), parathyroid hormone(PTH), Serum Protein electrophoresis, Calcium and vitamin D levels)
- Time to surgery in hours
- In hospital prescription of low molecular weight heparin(Enoxaparin)
- Inpatient or outpatient prescription of vitamin D and calcium
- Inpatient or outpatient prescription of anti-resorptive treatment

III. STUDY RELEVANCE

This study is aimed at determining our level of care for fragility fractures of the hip. It will identify weaknesses in our management strategies and recommendations will be made to improve our current treatment protocol.

IV. REPORT OF FINDINGS

The results will be submitted for publication in a peer review journal (South African Orthopaedic Journal) and will also be discussed at the South African orthopaedic congress and research or faculty meetings.

V. BUDGET AND FUNDING

Costs not requiring funding:

Departmental and personal computer usage.

Paper, stationery and photocopying supplied by the Orthopaedic department of the University of Cape Town.

Researchers will not be remunerated and will do the research as part of their current academic appointments.

VI. ETHICS

Informed consent is not applicable to this retrospective review, no patients identification will be linked to any of the raw data or results.

Risks/benefits:

There will be no risk or any potential benefit for the patients. The medical records will remain confidential. The results of this study will help us identify and strengthen deficient aspects of management of fragility fractures of the hip and the publication of these results could serve as a wake up call for other orthopaedic units around South Africa and the world to review their own treatment approach for fragility fractures of the hip.

VII. REFERENCES

1.Tp IP, Leung J, Kung AWC, Management of osteoporosis in patients hospitalized for hip fractures, Osteoporos Int(2010) 21(suppl4): S605-614.

2.Cassim B, Lipschitz S, Paruk F,Tipping B, Recommendations for the acute and long-term medical management of low trauma hip fractures, JEMDSA 2013;18(1):21-32.

3.Rabenda V,Vanoverloop J, Fabri V, Mertens R, Low incidence of anti-osteoporosis treatment after a hip fracture. J Bone Joint Surg Am. 2008;90:2142-8.

4. Robert KC, Brox WT, Jevsevar DS, Sevarino K, Management of hip fractures in the elderly. J Am Acad Orthop Surg 2015;**23**:131-137.

5. Jennings LA, Andrew D, Maselli J et al. Missed opportunities for osteoporosis treatment in patients hospitalized for hip fractures. J Am Geriatr Soc. 2010;**58**(4):650-657.

PART B: LITERATURE REVIEW

I. OBJECTIVES OF LITERATURE REVIEW

- To gain insight in the burden of fragility fractures of the hip (FFH) in terms of global prevalence, aetiology, current treatment guidelines and clinical outcome after treatment.
- To search for existing studies which have audited the management of FFH in various parts of the world.
- To gain knowledge and understanding of osteoporosis diagnosis, treatment and prevention.

II. SEARCH METHODOLOGY

Internet based search engines such as Pubmed, Medline and Google Scholar were used to identify articles relevant to the review. Articles were reviewed only if they were written in English and published in a peer reviewed journal.

Online relevant textbooks were also used.

III. INTRODUCTION

A fracture that is sustained following a minimal trauma such as a fall from standing height is defined as a fragility fracture. These fractures are caused by osteoporosis in its various forms. Fragility fractures of the hip constitute the most severe complication of osteoporosis because of the associated high mortality and morbidity rate.[1]

The incidence of FFH is expected to continue rising due to the ever increasing life expectancy seen in developed and emerging countries across the globe.[2]

It is estimated that 1 in 3 postmenopausal women and 1 in 5 men over the age of 75 will suffer a FFH in their life time. The rising global prevalence of FFH is estimated to reach 2.6 million in 2025 and 6.3 million by year 2050.[3]

FFH constitutes the most serious complication of osteoporosis carrying a mortality rate of up to 20 – 24% in the first year after injury and is associated with post injury decline in patients' level of activity in more than 50% of the cases.[2]

The understanding that patients affected by FFH often present with a background of significant medical co-morbidities and frailty has led to the development of strict management guidelines with emphasis on a multidisciplinary approach to improve survival rate and clinical outcome after a FFH.

The American Academy of Orthopaedic Surgeons clinical practice guidelines stipulate that surgical fixation of the hip fracture within 48 hours of admission coupled with multimodal pain treatment, DVT prophylaxis, frailty care and osteoporosis management will ensure a positive clinical outcome. The pre-surgery waiting time should only be allowed for medical management of unstable or uncontrolled co-morbid conditions.[5]

Studies have shown a tendency to neglect the management of osteoporosis and frailty in patients who have been treated for FFH at various orthopaedic centres across the world with only 2 to 8 % of these patients being referred for osteoporosis treatment.[4, 6]

While an in depth review of osteoporosis is outside the scope of this work, a summarized overview of osteoporosis is discussed in the subsequent sections of this review.

An integrated and multidisciplinary approach is highly desirable to ensure that medical co-morbidities are stabilised, the acute injury is adequately

treated and simultaneously osteoporosis is investigated and treatment initiated before the patient is discharged. This comprehensive approach will help decrease mortality and morbidity but also serves as a secondary prevention of subsequent fragility fractures for the patient under treatment.

It has been shown that such an approach is also cost effective in terms of preventing future hospital admissions for future fragility fractures.[7]

The orthopaedic surgeon is often the first point of contact and plays a key role in this multidisciplinary approach. He should think beyond surgical fixation of the fracture and invite relevant specialties on board at the initial patient's admission in the hospital.

IV. EATIOLOGY OF FRAGILITY FRACTURES OF THE HIP

The aetiology of fragility fractures of the hip (FFH) is multi-factorial. Osteoporosis represents the main aetiological factor and many other risk factors act together to predispose patients with osteoporosis to a fall from standing height or lower and fracture their hips.[8, 9]

These risks factors can be classified as follow:

1. Genetic susceptibility
    - Maternal FFH
    - Patient history of any fragility fracture
2. Risk factors for a fall
    - Cognitive impairment
    - Visual impairment
    - Balance and gait disorders
    - Sarcopenia
    - Use of certain medication
    - Presence of environmental hazards

V. OSTEOPOROSIS OVERVIEW

1. Definition

The term osteoporosis derives its etymology from a combination of 2 Greek words, osteo (bone) and poros (porous). It is used to describe a systemic skeletal disorder characterized by a decrease in bone mass and a progressive deterioration of the bone micro-architecture predisposing to fragility fractures.[10,11] The WHO has provided criteria for the diagnosis of osteoporosis and these criteria will be discussed under the diagnosis section of this overview.

2. Historical perspective

Sir Astlety Paston Cooper, a British Surgeon and Anatomist was the first to comment on the occurrence of fractures in subjects with abnormal bones in 1822. In 1835 the French pathologist and surgeon Jean Lobstein was the first to use the term osteoporosis to describe a condition associated with blue-grey sclera and weak bones which was probably osteogenesis imperfecta type I. In 1941 Fuller Albright described the cases of vertebral fractures and loss of height seen in women after loss of ovarian function. Oestrogen treatment restored calcium balance and prevented height loss.[12] These findings were the basis of the definition of postmenopausal osteoporosis and established a link between osteoporosis and vertebral fractures.

3. Risk factors for osteoporosis

It is important to recognize that the peak bone mass is achieved at age 25 to 30 and this is a crucial age group to maximize bone mass and strength. The peak bone mass achieved appears to be an important factor determining the severity and rate of bone mass decline in postmenopausal women after the age of 45 and men after the age of 50.[8,9]

Factors negatively impacting on peak bone mass include extremes of weight range (underweight and obesity), inadequate physical activity, smoking, multiple pregnancies in women.

Regardless of the peak bone mass the following risk factors will predispose to osteoporosis:

Age: after age 45 the ovarian function starts declining and oestrogen levels decline as well losing their protective effect on bone strength.

After the age of 75 the rate of fragility fractures increases significantly in both woman and men.[13] This is due to a higher rate of senile osteoporosis and frailty seen in this age group.

Sex: women are more affected by osteoporosis because of the combination of post-menopausal and senile osteoporosis.

Other factors: certain medical conditions such as celiac disease, renal disease, hyperparathyroidism, hypogonadism, inflammatory arthropathies and certain medications such as glucocorticoids will predispose patients to osteoporosis through various mechanisms.[10]

4. Clinical presentation and Diagnosis

Osteoporosis is asymptomatic and patients will only present with fragility fractures.[8] Trabecular bones will be affected early on and in the most severe forms cortical bone will be affected severely enough to predispose to fragility fractures. Patients will then fracture their wrists many years before they get to fracture their hips. It has been shown that the most common pattern is to fracture the wrist first, followed by vertebral compression fractures and lastly hip fractures. This is why certain authors have described osteoporosis as a silent killer.[14]

According to the WHO criteria, a diagnosis of osteoporosis is made when a patient has a T score lower than -2.5 or when a patient presents with a typical fragility fracture defined as a fracture occurring after a fall from standing height or lower and with clear osteopenia on plain radiographs.

A T score is obtained by measuring the patient bone mineral density (BMD) using a Dual-Energy X-ray Absorptiometry (DEXA) scan at the hip and the

spine and comparing it to a mean of young healthy Caucasian women.[9] Bone strength depends on bone density and bone quality. Only bone density can be measured at this stage and it is expressed as grams of mineral per scanned area (g/cm^2).[10]

Ideally Osteoporosis is diagnosed if the patient's T score is lower than -2.5 standard deviations below the mean of young healthy population matched for gender and ethnicity.[8,9] Due to lack of availability of data on mean bone mineral density for all ethnic groups the WHO allows matching the BMD of the patient to the mean BMD of young (21 to 29 year old) healthy white women.[8, 9, 10]

According to the WHO, a DEXA scan report should classify the patient in one of the 3 categories as follows[8]:

T score above -1 defines normal category

T score between -1 and -2.5 defines the osteopenia category

T score below -2.5 defines the osteoporosis category

5. Aetiological Classification of Osteoporosis

Osteoporosis is broadly classified in 2 major groups[10]:

Primary Osteoporosis: this group is further classified in 2 types. Type I osteoporosis defines the group of postmenopausal osteoporosis and type II defines the senile osteoporosis which affects patients after the age of 75.[8, 15]

Secondary Osteoporosis: this group defines osteoporosis due to a medical condition such as inflammatory and connective tissue disorders (rheumatoid arthritis, systemic lupus erythematous, etc..) or malignancies such as multiple myeloma, endocrinopathies such as hyperparathyroidism from various causes, hypogonadism, celiac disease and chronic use of certain drugs such as steroids.[8, 10]

6. Osteoporosis work-up

As a general rule osteoporosis investigations start with a DEXA scan which provides patient's T score to make a diagnosis and to have a baseline BMD to monitor the response to treatment.

Laboratory investigations will help exclude any possible causes of secondary osteoporosis and the following tests should be done for all patients under investigation for osteoporosis[10, 16]

1.ESR

2. TSH

3. PTH

4.Calcium levels

5.Vitamin D levels

6.Protein electrophoresis for a myeloma screen when clinically suspected.

7. Management of osteoporosis

7.1 General principles

Once the diagnosis has been made all efforts are directed at ruling out secondary causes of osteoporosis. The management plan will differ between the 2 main forms of osteoporosis namely primary and secondary osteoporosis.

General nutritional and lifestyle modifications will apply to both primary and secondary osteoporosis and include:

Regular physical activity

A daily intake of at least 1.2 g of calcium and 800 IU of vitamin D has been shown to reduce the relative risk of falls and fragility fractures mostly in the institutionalized elderly patients than in the community dwellers.[1, 17]

Adequate protein intake.

Smoking needs to be stopped and alcohol consumption moderated.

Pharmacological treatment will depend on the type of primary osteoporosis being addressed.

Postmenopausal osteoporosis will benefit from hormone replacement therapy early on but as senile osteoporosis sets in anti-resorptive therapy will be required to maintain adequate bone density.

7.2 Bisphosphonate therapy for osteoporosis

Bisphosphonates are synthetic, non-hydrolysable analogues of naturally occurring pyrophosphates that prevent loss of bone mass by interfering with osteoclastic activity.

The mechanism of action leading to inhibition of osteoclastic activity depends on the presence or absence of the nitrogen atom on the alkyl chain in the chemical structure on the drug.[17]

Non Nitrogen containing bisphosphonates (etidronate, clodronate, tiludronate) are the earlier generation and get incorporated into the osteoclast's adenosine triphosphate(ATP) inhibiting the formation of the osteoclast's ruffled border(required for bone resorption) and causing cell apoptosis to a certain degree. Higher doses are required to produce a significant clinical effect.

Nitrogen containing bisphosphonates (pamidronate, alendronate, risedronate, zolendronate) are the recent generation.

Nitrogen inhibits osteoclast's farnesyl pyrophosphate synthase (cholesterol pathway), GTPase and cellular membrane proteins phenylation causing cell apoptosis. Smaller doses produce a potent anti-resorptive activity. It is important to note that these nitrogen containing bisphosphonates differ in potency.[17]

Bisphosphonates can be administered orally or intravenously and have high affinity for hydroxyapatite adhering to bone surfaces in areas of high

turnover. They are ingested by osteoclasts and the non-ingested fraction is excreted by kidneys. Bone residency can last up to 10 years depending on the individual drug in use.[17]

For osteoporosis treatment oral bisphosphonates are administered either daily or weekly on an empty stomach and this can present a significant compliance challenge in the elderly patients. The most recent development of zolendronic acid (zolendronate) represents a very attractive option since it is given as a yearly intravenous injection, very appealing for the elderly patients to eliminate compliance issues.[18]

In the setting of osteoporosis bisphosphonate therapy is indicated for patients with a T score below -2.5(lower than -2.5 standard deviations), those with a T score between –1 and -2.5 and additional risk factors for fragility fractures, patients presenting with recognized fragility fractures after exclusion of secondary causes, patients with a ten- year risk of hip fracture of ≥3% or a ten- year risk of major osteoporosis related fractures of ≥20% as calculated by the applicable Fracture Risk Assessment Tool (FRAX) [17,18]. The FRAX tool combines patient's specific bone mineral density and clinical risk factors such as age, gender, body mass index(BMI), history of fragility fractures, history of maternal hip fracture and current smoking status to calculate a ten-year probability or risk of a hip or other osteoporosis related fractures for each patient. The FRAX index is specific for each country.[19] Most common prescription include either Alendronate 70 mg weekly or zolendronic acid 5mg IV yearly.[16]

The fracture risk reduction expected with the use of bisphosphonates has been widely studied on patients with vertebral fragility fractures. Alendronate has proven to reduce the vertebral fracture risk by 60%.[17]

The most compelling data about the hip fracture risk reduction comes from the HORIZON(Health Outcomes and Reduced Incidence with zolendronic Acid Once Yearly) trial on the use of yearly 15 minute intravenous infusions of 5mg zolendronic acid started within 90 days after fixation of fragility fractures of the hip.[20] The pivotal HORIZON study showed a 70% risk reduction of morphometric vertebral fractures and 41% risk reduction of hip

fractures at 36 months with an improved overall quality of life and a reduction in mortality rate. Patients treated with zolendronic acid were less likely to die of pneumonia and arrhythmias than placebo treated patients.[20]
The mechanism underlying the later findings has not been clearly explained.

Beside the oesophageal and gastro-intestinal upset that oral bisphosphonates can cause, the most feared side effects of bisphosphonates include atypical femur fractures, osteonecrosis of the jaw and delayed or impaired fracture healing.[17, 18]

Atypical femur fractures

The 2013 American Society for Bone and Mineral Research Task Force Revised Case Definition of Atypical Femur Fractures provides major and minor criteria for the diagnosis of atypical femur fracture.[17]

Major criteria

The fracture is a low energy fracture due to no trauma or minimal trauma as a fall from standing height or less.

The Fracture line starts from the lateral cortex and is essentially transverse in its orientation but can become oblique as it progresses to the medial cortex.

Complete fractures are not comminuted and may be associated with a medial spike and there is thickening of the lateral cortex at the fracture site.

The fracture must be located either in the sub-trochanteric area or in the diaphysis between the sub-trochanteric area and the supracondylar flare.

Minor criteria

Unilateral or bilateral prodromal groin or thigh pain

Generalized increase in diaphyseal cortex thickness

Bilateral complete or incomplete fractures

Delayed fracture healing

At least 4 major criteria need to be met to make the diagnosis of atypical femur fracture. Minor criteria will just strengthen the suspicion[15].

The rate of these fractures varies in the literature but the known fact is that the incidence shows an exponential increase with the increase in the number of years of continuous treatment. Data from Kaiser California reported an age adjusted incidence of 1.8 per 100,000 with up to 2 years of bisphosphonates use, 16 per 100,000 with 4 - 6 years of use and 107, 5 per 100,000 with more than 10 years of use.[18]

To prevent the occurrence of atypical fractures the concept of “drug holiday” has been introduced. This concept is based on the fact that bisphosphonates activity last many years after the treatment has been interrupted.[15] It has been shown that after 5 years of Alendronate treatment osteoclastic activity remains inhibited for an additional 5 years[18] and zolendronic acid activity continues for an additional 3 years after 3 years of use.[18]

The initiation time of drug holiday and its duration still is a debatable issue and this should vary with the particular bisphosphonate being used and patient’s additional risk factors.

Recommendations for drug holiday from bisphosphonates

High risk: T- score ≤ -2.5 at the hip, previous fracture of the hip or spine or ongoing high dose glucocorticoid: drug holiday not justified but reassess the need for treatment at regular intervals.

Moderate risk: T score ≥ -2.5 at the hip, no prior history of hip or spine fragility fracture, consider drug holiday after 3 to 5 years of treatment with alendronate, risedronate and zolendronic Acid.[17]

Osteonecrosis of the jaw

Osteonecrosis of the jaw is defined in 2 stages. In the preclinical stage the diagnosis is radiographic and based on the appearance of the mandible on plain radiographs. In the clinical stage the diagnosis is made on

demonstration of an area of exposed bone in the oral cavity that fails to heal within 8 weeks of treatment.[18]

The rate of osteonecrosis of the jaw is higher in the patients treated with bisphosphonates in the oncology department than for those treated for osteoporosis. This underlines the fact that the incidence is probably influenced by the combination of bisphosphonates and anti-neoplastic agents such as angiogenesis inhibitors and immuno-suppressors. In the osteoporosis treatment group the rate of osteonecrosis of the jaw is much lower than that of atypical femoral fractures.[18, 20]

Impaired fracture healing

Bisphosphonates interfere with the course of continuous bone remodelling and it is logical to think that in so doing bisphosphonates may impair bone healing. This logical concern has not been validated in the literature.

A meta-analysis of 8 randomized controlled trials including 2,508 patients found no statistically significant difference in bone healing at short term (3 months) or long term (more than 12 months) between bisphosphonates infusion groups and control groups. There were no statistically significant differences in indirect bone healing between the early bisphosphonates groups and delayed bisphosphonates groups. Bisphosphonates infusions post lumbar fusion surgery increased fusion rates and shortened time to fusion to 6 months post-operative[21].

Other recent pharmacological agents for the treatment of Osteoporosis

Parathyroid hormone (Forteo)

While known to induce bone resorption and hypercalcemia intermittent low doses of parathyroid hormone have shown an anabolic effect on bone metabolism promoting bone formation.[22]

Pulsatile low dose parathyroid hormone is indicated for resistant osteoporosis and calcium levels must be monitored during treatment. It is contraindicated in patients with history of Paget disease because of its potential for malignant transformation.[22]

Denosumab (Prolia, Amgen)

This recent pharmacological agent is a RANKL (receptor activator of nuclear factor-Kappa B ligand) antibody which inhibits osteoclastic activity. The Fracture Reduction Evaluation with denosumab Once 6 Monthly (FREEDOM) trial indicated that unlike bisphosphonate denosumab has a rapid onset of osteoclastic inhibition and bone turn over reverses soon after discontinuation of treatment.[23] It is administered as a subcutaneous injection six-monthly and indicated as an alternative to bisphosphonates in the first line of treatment of osteoporosis.

Strontium Ranelate (Protos)

This is a strontium salt which activates osteoblastic activity and inhibit osteoclastic activity resulting in net bone formation. It is used as a daily oral suspension and indicated for first line treatment of patients who are not suitable for bisphosphonates or denosumab. Concerns about its cardiovascular safety profile have not been validated in current literature.[24]

VI. STANDARD OF CARE FOR FRAGILITY FRACTURES OF THE HIP

The aim of treatment of fragility fractures of the hip is to restore the patient's pre-injury activity level while minimizing morbidity and mortality and to lay out a plan for secondary prevention of future fragility fractures.

A multidisciplinary approach is required to cater for the wide variety of physiological disturbances that are often present and requiring treatment.

From the moment the patient is first seen in the emergency room all necessary investigations are conducted, hydration status corrected and co-morbidities controlled with the aim to get the patient to theatre within 48

hours. In a prospective observational study Pioli et al have shown that the one year mortality risk increased by 12% per day of surgical delay.[25]

The emergency physician would usually refer these patients straight to the orthopaedic surgeon and the latter becomes a key player in the multidisciplinary team that will be looking after these patients.

A review article by Ekman gives a check list of management priorities that the orthopaedic surgeon must satisfy while treating fragility fractures of the hip. This check list ensures that the patient receives a holistic, comprehensive treatment for a positive outcome.[26]

The multidisciplinary approach is aimed at reducing the perioperative complications seen in patients being treated for fragility fractures of the hip. These complications include DVT, pulmonary infections, delirium, decubitus pressure ulcers and cardiovascular events.

The current recommendations for the treatment of fragility fractures of the hip include

1. Specialized pain management.
2. DVT prophylaxis
3. Early surgery(within 48-72 hours of injury)
4. Early physical therapy and nutritional interventions
5. Referral to geriatricians and endocrinologists for the management of frailty and osteoporosis.

A single centre study has shown that initiation of a standardized pain control program including the pre-operative use of femoral nerve blocks, avoidance of general anaesthesia and liberal use of oral intakes(food and oral fluids) pre-operatively resulted in much lower rate of peri-operative complications (pneumonia, urinary tract infection, delirium) compared to pre-program rates.[27]

A meta-analysis of prospective cohorts in Asian patients with hip fractures reported a DVT rate of 26% when prophylaxis was not used.[28] It is therefore recommended that all patients receive effective DVT prophylaxis.

A quarter of patients admitted with fragility fractures will develop delirium. Predisposing factors for delirium include male gender, multiple co-morbidities, low body mass index, prolonged surgery and general anaesthesia.[29] Although post-operative delirium is usually transient, it will persist for more than 4 weeks in 20% of patients. Importantly delirium is associated with lower functional recovery and higher mortality rate at 1 year.[30] Therefore the prevention of delirium becomes of paramount importance.

The literature supports that early referral to geriatricians is associated with lower rate of postoperative delirium. The geriatrician will also assess the risk of future falls and implement strategies to minimize or prevent falls. Factors such as delirium, use of psychoactive pain control agents, frequent change of care locations increase the risk of future falls and need to be addressed.[30,31,32]

Sarcopenia is being increasingly recognized as an independent risk factor for falls and fragility fractures. It is defined by the presence of a low skeletal muscle mass and strength with poor physical performance.[33]

Physiotherapists and dieticians work together to correct sarcopenia and optimize physical performance of these patients for a better clinical outcome.

It is the orthopaedic surgeon's responsibility to make early and appropriate referrals to geriatricians, physicians, endocrinologists, physical therapists and dieticians. These other team players will help optimize patient's medical condition to allow early surgery, early rehabilitation, optimal investigations, prevention and treatment of peri-operative complications and lay out a plan for osteoporosis treatment.

The orthopaedic surgeon is encouraged to go beyond the acute fracture care and ensure that osteoporosis is investigated and treated either by him/her or by his/her medical parteners.[34]

The current literature shows that, for various reasons, less than 10% of patients presenting to major trauma centres with fragility fractures of the hip actually get a full evaluation and management of osteoporosis. [6, 34, 35,36]

This outlines a need to increase awareness of osteoporosis management in orthopaedic trauma centres.

Further studies need to be directed at ways of preventing the first fragility fracture of the hip. Devices such as hip protectors are being developed and tested.[37] Newer pharmacological agents such as cathepsin K inhibitors are being slowly introduced for the management of osteoporosis.[38]

Cathepsin K is the protease that is primarily responsible for bone matrix resorption caused by osteoclasts. Selective inhibition of cathepsin K theoretically affects only one function of osteoclasts leaving their stimulation of bone formation unaffected. Cathepsin K inhibitors are claimed to not only prevent bone resorption but also to promote bone formation.[38]

VII. References

1. Tp IP, Leung J, Kung AWC. Management of osteoporosis in patients hospitalized for hip fractures. Osteoporos Int 2010;**21**(4): S605-614.

2. Cassim B, Lipschitz S, Paruk F, Tipping B. Recommendations for the acute and long-term medical management of low trauma hip fractures. JEMDSA 2013;**18**(1):21-32.

3. Cooper C, Campion G, Melton LJ 3rd. Hip fractures in the elderly: a worldwide projection. Osteoporosis Int. 1992;**2**(6):285-289.

4. Rabenda V, Vanoverloop J, Fabri V, Mertens R. Low incidence of anti-osteoporosis treatment after a hip fracture. J Bone Joint Surg Am. 2008; **90**:2142-8.

5. Robert KC, Brox WT, Jevsevar DS, Sevarino K. Management of hip fractures in the elderly. J Am Acad Orthop Surg 2015;**23**:131-137.

6. Jennings LA, Andrew D, Maselli J et al. Missed opportunities for osteoporosis treatment in patients hospitalized for hip fractures. J Am Geriatr Soc. 2010;**58**(4): 650-657.

7. Swart E, Vasudeva E, Bozic J. Dedicated Perioperative Hip Fracture Co-management Programmes are Cost effective in High volume Centers: An economic analysis. Clin Orthop Relat Res 2016;**474**:222-233. 17. Lorentzon M, Cummings SR. Osteoporosis: the evolution of a diagnosis. J Intern Med 2015;**277**: 650–661.

8. Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. *N Engl J Med* 1988; **319:** 1701-1707.

9. Lorentzon M, Cummings SR. Osteoporosis: the evolution of a diagnosis. J Intern Med 2015;**277**: 650–661.

10. Hough S. Osteoporosis in South Africa. Chronic Diseases of Lifestyle in South Africa since 1995-2005; **13**:186-193.

11. NIH Consensus Panel Development on osteoporosis Prevention, Diagnosis and therapy. JAMA 2001; **285**(6): 785-795.

12. Albright F, Burnett C, Cope O. Acute atrophy of bone(osteoporosis) simulating hyperparathyroidism. J Clin Endocrinol metab 1941; **1**: 711-716

13.Felsenberg D, Silman AJ, Lunt M et al. Incidence of vertebral fracture in europe: results from European Prospective Osteoporosis Study(EPOS). J Bone Miner Res 2002;**17:**716-724.

14. Chang SF, Hong CM, Yang RS. the performance of an online osteoporosis detection system. Specificity and sensitivity analysis. Journal of clinical nursing 2014;**23**: 1803-1809.

15. Riggs BL, Melton LJ 3rd. Evidence for two distinct syndromes of involutional osteoporosis. Am J Med.1983;**75:**899-901.

16. Strotman P, Lack W, Bernstein M. Evaluation of common fractures of the hip in the elderly. Cuur Geri Rep 2016;**5**:38-43.

17. Balach T, Paul C, Baldwin, Intravia J. Atypical Femur Fractures Associated with diphosphonate use. J Am Acad Orthop Surg 2015;**23**: 550-557.

18. Reyes C, Hitz M, Alhambra DP, Risks and benefits of bisphosphonates therapies, J. Cell. Biochem 2016;**117**:20-28.

19. Unnanuntana A, Gladnick BP, Lane JM. The assessment of fracture risk. J Bone Joint Surg Am. 2010;**92**(3):743-753.

20. Keneth W, Cathleen S, Jay S, Jonatha D, Carl F, Carlos M. Zolendronic Acid and Clinical fractures and Mortality after Hip Fracture. N Engl J Med 2007;**357**: 1799-809.

21. Deting X, Fangcai L, Gang C, ShiguiY, Zhijun P. Do bisphosphonates affect bone healing? A meta-analysis of randomized controlled trials. Journal of orthopaedic surgery and research. 2014;**9**:1-45.

22. Morley P, Whitefield JF, Willick GE. parathyroid hormone; an anabolic treatment for osteoporosis. Curr pharm Des 2001;**7**(8)671-87.

23. Silverman SL. New therapies for osteoporosis: Zolendronic acid, Bazedoxifene and Denosumab. Current Osteoporosis Report 2009;**7**:91-95.

24. Atteritano M, Catalano A, Santoro D, Lasco A, Benvenga S. Effects of Strontium Ranelate on markers of cardiovascular risk in postmenopausal osteoporotic women. Endocrine 2016;**53**(1):305-312.

25. Pioli G, Frondini C, Lauretani F at al. Time to surgery and rehabilitation resources affects outcomes in ortho-geriatric units. Archives of Gerontology and Geriatrics. 2012;**55**: 316-322.

26. Ekman EF, the role of the orthopaedic surgeon in minimizing mortality and morbidity associated with fragility fractures. J Am Acad Orthop Surg. 2010;**18**:278-285.

27. Borgbjerg FM, Schousboe B, Pedersen SJ et al, A comprehensive hip fracture program reduces complications rate and mortality, J Am Geriatr Soc 2008;**56**:1831-1838.

28.Kanchanabat B, Stapanavatr W, Meknavin S, Soorapanth C, Sumanasrethakul C, Kanchanasuttirakn P. Systematic review and meta-analysis on the rate of postoperative venous thrombo-embolism in orthopaedic surgery in Asian patients without thrombo-prophylaxis. Br J Surg. 2011;**98**:1356-1364.

29. Lee HB, Mears SC, Rosenberg PB, Leoutsakos J-MS, Gottschalk A, Sieber FE. Predisposing factors for postoperative delirium after hip fracture repair in individuals with and without dementia. J Am Geriatr Soc 2011;**59**:2306-2313.

30. Lee K-H, Ha Y-C, Lee Y-K, Kang H, Koo K-H. Frequency, risk factors, and prognosis of prolonged delirium in elderly after hip fracture surgery. Clin Orthop Relat Res. 2011;**469**:2612-2620.

31. Marcantonio ER, Flacker JM, Wright RJ, Resnick NM. Reducing delirium after hip fracture: a randomized trial. J Am Geriatr Soc 2001;**49**:516–522.

32.Deschodt M, Braes T, Flamaing J, Detroyer E, Broos P, Haentjens P et al. Preventing delirium in older adults with recent hip fracture through multidisciplinary geriatric consultation. J Am Geriatr Soc 2012;**60**:733–739.

33. Bokshan SL, DePasse JM, Daniels AH. Sarcopenia in orthopaedic surgery. Orthopedics 2016;39(2):e295-e300.

34. Mary Bouxsein L, Kaufman J, Laura T. Recommendations for optimal care of fragility fracture Patients to reduce the risk of future fractures. J Am Acad Orthop Surg 2004;**12**: 385-395.

35. Majumdar SR et al, Recent trends in osteoporosis treatment after hip fracture: Improving but wholly inadequate. J. Rheumatol. 2008;**35**:190-191.

36. Kaufman JD, Bolander ME, Bunta AD, et al. Barriers and solutions to osteoporosis care in patients with a hip fracture. J Bone Joint Surg Am. 2003;**85**:1837-42.

37. Cianferotti L, Fossi C, Brandi ML. Hip protectors: are they worth it? Calcif tissue Int. 2015;**97**:1-11.

38. Boonen S, Rosenberg E, Claessens F, Vander schueren D, Papapoulos S. Inhibition of cathepsin K for treatment of osteoporosis. Curr Osteoporos Rep.2012;**10**(1):73-79.

C. MANUSCRIPT (PUBLICATION READY FORMAT)

THE MANAGEMENT OF FRAGILITY FRACTURES OF THE HIP: A QUALITY ASSESSMENT PROJECT

N Kauta (MBChB), M Held(FC ortho), S Dlamini(FCP), S Kalula(FCP), I Ross (FCP), G Kalla(FCP), S Maqungo(FC ortho)

Groote Schuur Hospital, University of Cape Town

Department of Orthopaedic Surgery

Department of Infectious diseases

Department of Geriatrics

Department of Endocrinology

Department Rheumatology

Correspondence: Dr N KAUTA

PO BOX 1293

MOWBRAY

7700

Jimmykauta@gmail.com

Cell: 071 896 2589

Work: 021 404 5108

Abstract

Fragility fractures of the hip (FFH) constitute the most serious complication of osteoporosis carrying a mortality rate of up to 30% in the first year after injury. Less than 50% of affected patients will regain their pre-injury activity level.

Surgical fixation of the hip fracture within 48 hours of injury, multimodal pain management, deep vein thrombo-prophylaxis, early physical therapy and simultaneous management of osteoporosis and frailty in a multidisciplinary approach constitute the standard of care for FFH to keep the mortality and morbidity rates as low as possible and prevent future fragility fractures.

Aim

To assess the standard of care of FFH at our institution and determine areas of management which require more attention and improvement.

Methods

Retrospective review of clinical and radiographic records of all patients admitted at our institution for fragility fractures of the hip from 1st January 2014 to 31st December 2014.

The waiting time from admission to surgical fixation of the hip fracture, pain control and thrombo-prophylaxis strategies, rate of geriatric referrals and extent of osteoporosis management were assessed.

Results

We admitted 113 fragility fractures of the hip from 1st January to 31st December 2014, 98 clinical records and 98 pelvis radiographs were included in the study. The other 15 clinical records were incomplete and were therefore excluded.

The average waiting time from admission to surgery was 49 hours (range 9 - 120). All patients received low dose morphine, paracetamol and tramadol for perioperative pain control. Low molecular weight heparin and compression stockings were prescribed for thrombo-prophylaxis in all patients.

Only 2 (2, 04%) patients had some osteoporosis investigations ordered and none of the patients were referred to the geriatric department, none of them were formally treated for osteoporosis.

Conclusion

While the waiting time from admission to surgery was largely within the recommended time frame, there were no signs of a multidisciplinary approach to the management of fragility fractures of the hip at our institution leaving osteoporosis and frailty largely untreated.

Key words: fragility fractures, hip, geriatric hip fractures, standard of care for hip fractures, osteoporosis, frailty care

Introduction

A hip fracture that is sustained following a minimal trauma such as a fall from standing height is defined as a fragility fracture of the hip (FFH). Fragility fractures of the hip are caused by osteoporosis in its various forms and constitute the most severe complication of osteoporosis because of the associated high mortality and morbidity rates.[1]

The incidence of FFH is expected to continue rising due to the ever increasing life expectancy seen in developed and emerging countries across the globe.[2]

It is estimated that 1 in 3 postmenopausal women and 1 in 5 men over the age of 75 will suffer a FFH in their life time. The rising global prevalence of FFH is estimated to reach 2.6 million in 2025 and 6.3 million by year 2050[2].

FFH carry a mortality rate of up to 30% in the first year after injury and are associated with a post injury decline in patients' level of activity in more than 50% of the cases.[2,3] These factors make FFH the most serious complication of osteoporosis.

The understanding that patients affected by FFH often present with a background of heavy medical co-morbidities and medical frailty has led to the development of strict management guidelines with emphasis on a multidisciplinary approach to improve survival rate and clinical outcome after a FFH.

The American Academy of Orthopaedic Surgeons clinical practice guidelines stipulate that surgical fixation of the hip fracture within 48 hours after injury coupled with multimodal pain treatment, deep vein thrombosis(DVT)prophylaxis, frailty and osteoporosis management will ensure a positive clinical outcome. The pre-surgery waiting time should only be allowed for medical management of unstable or uncontrolled co-morbid conditions.[4]

Studies have shown a tendency to neglect the management of osteoporosis and frailty in patients who have been treated for FFH at various orthopaedic centres across the world with only 2% to 8 % of these patients being referred for osteoporosis treatment.[5,6]

Osteoporosis is broadly classified in 2 major groups[7]:

Primary Osteoporosis: this group is further classified in 2 types. Type I osteoporosis defines the group of postmenopausal osteoporosis and type II defines senile osteoporosis which affects patients after the age of 75.[8,9]

Secondary Osteoporosis: this group defines osteoporosis due to a medical condition such as inflammatory and connective tissue disorders (rheumatoid arthritis, systemic lupus erythematosus, etc…) or malignancies such as

multiple myeloma, endocrinopathies such as hyperparathyroidism from various causes, hypogonadism, celiac disease and chronic use of certain drugs such as steroids.[7,8]

It is vitally important that osteoporosis, the main etiological factor of FFH be appropriately investigated and classified to initiate appropriate treatment.

Alongside osteoporosis many other risk factors play a significant role in causing FFH. These factors need to be identified at the initial admission and appropriate measures taken to prevent further falls and fractures. These risk factors include cognitive impairment, visual impairment, balance and gait disorders, sarcopenia, use of neuroactive medication, history of maternal FFH, patient's history of any fragility fracture.[8,10]

An integrated and multidisciplinary approach is highly desirable to ensure that medical co-morbidities are stabilised, the acute injury is adequately treated and simultaneously osteoporosis is investigated and its treatment initiated before the patient is discharged.

This comprehensive approach will decrease mortality and morbidity and ensure secondary prevention of subsequent fragility fractures.

The purpose of this study was to assess the standard of care of FFH at our Institution and identify areas of management that require improvement.

Patients and methods

We conducted a retrospective review of clinical and radiographic records of all patients admitted with a fragility fracture of the hip at our level 1 trauma unit from 1st January 2014 to 31st December 2014.

Patients' details were obtained from our admissions records and matched with details on our surgical database. We were able to retrieve their folders from our records department and their radiographs were available on our digital PACS (picture archiving and communication system).

Only fractures sustained due to falling from standing height or lower (bed or chair) with radiographic osteopenia were included.

Pathological and high energy fractures were excluded.

Incomplete clinical records were excluded.

We examined clinical records to determine the waiting time from admission to surgery, pain control and thrombo-prophylaxis strategies, the rate of geriatric referrals and the extent of evaluation and management of osteoporosis. Formal evaluation of osteoporosis meant that serum Vitamin D, calcium levels, erythrocyte sedimentation rate, thyroid function test and parathyroid hormone level were all requested with or without a DEXA scan.

Ethical approval was obtained from our institution's Human Research Ethics Committee.

Results

We admitted 113 fragility fractures of the hip from 1st January to 31st December 2014, 98 clinical records and 98 pelvis radiographs were included in the study. The other 15 clinical records were incomplete and were therefore excluded. Eighty- three patients (84.7%) were females and 15 (15.3%) were males (fig1). The mean age was 71.6 years (range 40 - 93) (fig2). The average waiting time from admission to surgery was 49 hours (range 9-120). All patients had low dose morphine, tramadol and paracetamol prescribed for pain control. They all had low molecular weight heparin 40 mg subcutaneously and compression stockings prescription for thrombo-prophylaxis. Two patients (2.04%) had a DEXA scan done for bone mineral density assessment but none of the patients were formally investigated for osteoporosis. No patient had a vitamin D or calcium prescription in hospital or on subsequent visits. Bisphosphonates were not prescribed for any of the patients and none of the patients were referred to the geriatric department.(fig3)

Fifteen (15.3%) patients presented with a history of a previous fragility fracture of the contra-lateral hip and 2 of them had 2 previous major fragility

fractures (spine and proximal humerus fractures) without any previous assessment or management of osteoporosis.

Discussion

The results of this study have emphasised that fragility fractures are not only an injury of the female gender but males also can be affected. In our study 15% of cases were males. On further analysis 3% of the patients who were under 50 years of age were males. Despite their lower incidence of fragility fractures male patients tend to have poorer outcomes compared to postmenopausal women.[11]

The aim of treatment of fragility fractures of the hip is to restore the patient's pre-injury activity level while minimizing morbidity and mortality and laying out a plan for secondary prevention of future fragility fractures.

To achieve this aim a multidisciplinary approach is required to cater for the wide variety of physiological disturbances that are often found in these patients.

The emergency physician would usually refer these patients straight to the orthopaedic surgeon and the later becomes a key player in the multidisciplinary team that will be looking after these patients.

Ekman in his review article gives a check list of management priorities that the orthopaedic surgeon must satisfy while treating fragility fractures of the hip. This check list ensures that patients receive a holistic treatment for a positive outcome.[12]

The multidisciplinary approach is aimed at reducing peri-operative complications seen in patients being treated for fragility fractures of the hip. These complications include Deep Vein Thrombosis (DVT), pulmonary infections, delirium, decubitus pressure ulcers and cardiovascular events.

The current recommendations for the treatment of fragility fractures of the hip involve a specialized pain management strategy, thrombo-prophylaxis, early surgery (within 48 hours of admission), referral to geriatricians, physical therapists, dieticians and endocrinologists for a multidisciplinary care.[4]

The results of our study show that there was urgency in the surgical management of FFH with an average waiting time of 49 hours from admission to surgery. Patients who did not require advanced cardiopulmonary investigations for their pre-operative work up could get to theatre within 9 hours of admission into hospital. However patients who required extensive cardiopulmonary evaluation and stabilization could wait up to 120 hours. Our waiting time to surgery signals that our casualty personnel, orthopaedic surgeons and anaesthetists understand the urgency to surgically stabilise these fractures and allow early rehabilitation.

Special investigations such as cardiac echography and lung function test constituted the major reasons for delayed surgical fixation of the hip fracture. Patients admitted on a Friday evening would wait till the next Monday for a cardiac echography or a lung function test to be done if necessitated by their cardiopulmonary conditions.

In a prospective observational study Pioli reported that the one year mortality risk increased by 12% per day of surgical delay.[13] It is therefore imperative that all unnecessary delays to surgery be proactively avoided to prevent morbidity and mortality.

All our patients had low dose morphine, tramadol and paracetamol prescription for pain control. This conservative approach undertreats pain and predisposes to pain induced delirium. In a single centre study, initiation of a standardized pain control program including the pre-operative use of femoral nerve blocks, avoidance of general anaesthesia and liberal use of oral intakes (food and oral fluids) pre-operatively resulted in much lower peri-operative complications (pneumonia, urinary tract infection, delirium) compared to pre-programme rates.[14]

Deep vein thrombosis (DVT) is another major complication that must be prevented in this fragile population of patients. A meta-analysis of prospective cohorts in Asian patients with hip fractures revealed that 26% of patients not on DVT prophylaxis developed a postoperative DVT.[15] It is therefore recommended that all patients receive effective DVT prophylaxis.

All our patients had low molecular weight heparin (Enoxaparin 40 mg once daily subcutaneously) prescribed for DVT prophylaxis. This was combined with a prescription of compression stockings for all patients.

Fifty-one percent of reviewed cases were patients above the age of 75. In this age group the incidence of fragility fracture rises significantly.[16] This probably due to a combination of frailty and senile osteoporosis. These patients need to be seen by a geriatrician who will optimise their medical condition while the orthopaedic surgeon focuses on surgical treatment. None of our patients were referred to a geriatricians.

A quarter of patients admitted with fragility fractures will develop delirium.[17] Predisposing factors for delirium include male gender, multiple co-morbidities, low body mass index (BMI), prolonged surgery and general anaesthesia.[17] Post-operative delirium is usually transient but it can persist for more than 4 weeks in 20% of patients. Delirium is associated with lower functional recovery and higher mortality rate at 1 year.[18] Therefore the prevention of delirium becomes of paramount importance.

The literature supports that early referral to geriatricians is associated with lower rate of postoperative delirium.[19,20] Where the service of a geriatrician is lacking a specialist physician with interest in the field of geriatrics can be consulted for the management of these patients.

By definition a FFH implies a diagnosis of osteoporosis. According to the WHO criteria, a diagnosis of osteoporosis is made when a patient has a T score lower than -2.5 or when a patient presents with a typical fragility fracture defined as a fracture occurring after a fall from standing height or lower and has osteopenia on plain radiographs.[8] This definition excludes pathological fractures due to malignancies and infections. Osteoporosis must be investigated, classified and appropriately treated for every patient presenting with a FFH.

In our study only 2 out of 98 patients had a DEXA scan done with no other osteoporosis investigations ordered. None of our patients were treated for osteoporosis. This finding outlines the fact that orthopaedic surgeons satisfy themselves with a well performed fracture fixation as seen on postoperative radiographs and forget to facilitate or initiate the management of frailty and osteoporosis.

Similar studies conducted in Europe and in the United States have reported the same trend. Very few patients presenting with fragility fractures of the hip will actually get treated for osteoporosis. Rabenda et al reported that only 4.6% of patients with fragility fractures of the hip were fully treated for osteoporosis in their study[4] and Jennings reported a 2% rate of osteoporosis treatment in patients admitted for fragility fractures of the hip.[6]

Osteoporosis work up starts with a DEXA scan which provides patient's T score for the diagnosis and a baseline bone mineral density(BMD) to monitor response to treatment. However the lack of a DEXA scan should not hinder osteoporosis treatment for patients presenting with FFH.

Laboratory investigations will help exclude any possible cause of secondary osteoporosis and the following tests should be requested for all patients under investigation for osteoporosis:[7, 21]

1.Erythrocyte sedimentation rate (ESR)

2.Thyroid function test

3.Serum parathyroid hormone (PTH) level

4.Serum calcium level

5.Vitamin D level

6.Protein electrophoresis for a myeloma screen when clinically suspected.

The management plan will differ between the 2 main forms of osteoporosis, namely: primary and secondary osteoporosis.

General nutritional and lifestyle modifications will apply to both primary and secondary osteoporosis and include regular physical activity, adequate intake of calcium, vitamin D and proteins.

A daily intake of at least 1.2g of calcium and 800 IU of vitamin D has been shown to reduce the relative risk of falls and fragility fractures more in the institutionalized elderly patients than in the community dwellers.[1, 22]

Sarcopenia is being increasingly recognized as an independent risk factor for falls and fragility fractures.[23] Physiotherapists and dieticians work together to correct sarcopenia and optimize physical performance of these patients for a better clinical outcome.

Smoking needs to be stopped and alcohol consumption moderated.

Pharmacological treatment will depend on the type of primary osteoporosis being addressed.

Postmenopausal osteoporosis may benefit from hormone replacement therapy early on but as senile osteoporosis sets in bisphosphonates therapy will be required to maintain adequate bone mineral density.

Once all causes of secondary osteoporosis have been excluded bisphosphonate therapy is indicated. High risk patients as determined by the applicable Fracture Risk Assessment Tool (FRAX index) are also eligible for treatment [22,24]. The FRAX tool combines patient's specific bone mineral density and clinical risk factors such as age, gender, body mass index(BMI), history of fragility fractures, history of maternal hip fracture and current smoking status to calculate a ten-year risk of hip or other osteoporosis related fractures for the patient being assessed. This tool is country specific.[24]Most commonly oral alendronate 70 mg weekly or zolendronic acid 5mg IV yearly is prescribed.[25]

Alendronate has been proven to reduce the vertebral fracture risk by 60% and hip fracture risk by 30%.[25] Zolendronic acid once yearly study showed a 70% risk reduction of morphometric vertebral fractures and 41% risk reduction of hip fractures at 36 months.[26]

The most debated side effects of bisphosphonates are atypical femur fractures, osteonecrosis of the jaw and delayed or impaired fracture healing.[22,25]

The rate of atypical femur fractures varies in the literature but the known fact is that the incidence shows an exponential increase with the increase in the number of years of continuous bisphosphonates treatment.[25]

Osteoclastic activity remains inhibited for a few years after discontinuation of bisphosphonates use. This allows for a “drug holiday” to minimise the rate of atypical fractures.[26]

In the setting of osteoporosis treatment , the rate of osteonecrosis of the jaw is much lower than that of atypical femoral fractures.[25, 26]

A meta-analysis of 8 randomized controlled trials found that bisphosphonate treatment did not impair or delay fracture healing at short term (3 months) or long term (more than 12 months).[27]

Other recent and not widely available pharmacological agents for the treatment of osteoporosis include parathyroid hormone (Forteo, Teriparatide), Denosumab (Prolia), Strontium Ranelate (Protos) and Cathepsin K inhibitors.[28,29,30,31]

To simply provide a sound and early surgical fixation of the hip fracture and not address the underlying osteoporosis, frailty and certain possible causes of falls is in a way failing to provide the holistic and comprehensive management that these patients need.

The orthopaedic surgeon is most often the first specialist to see these patients and it is his or her responsibility to make early and appropriate referrals to geriatricians, physicians, endocrinologists, physical therapists and dieticians. These other team players will help optimize patients’ medical condition to allow early surgery, early rehabilitation, optimal investigations, prevention and treatment of peri-operative complications and lay out a plan for osteoporosis treatment.

The literature shows that less than 10% of patients presenting to major trauma centres with fragility fractures of the hip are fully evaluated and managed for osteoporosis. This outlines the need to increase awareness of osteoporosis management in orthopaedic trauma centres worldwide.[4,6,32]

This study was the first step of our quality assessment project for the management of fragility fractures of the hip at our institution. It has led to the development of a strict management protocol and the genesis of an ortho-geriatric unit called GOGO (Geriatric Orthopaedic and Generalized Osteoporosis) that functions as our fracture liaison service for a focused and improved care for fragility fractures of the hip as the primary target.

The ortho-geriatric unit aims at providing an integrated service where orthopaedic surgeons and geriatricians provide an integrated care without the frustration of lengthy telephonic referrals. Geriatricians see these patients as their own patients and not as orthopaedic patients.

There are various models of integrated fragility fracture care available, each institution treating these fractures should adopt a suitable model that promotes an integrated multidisciplinary approach and optimal treatment of these fragile patients for secondary prevention of fragility fractures.

CONCLUSION

The vast majority of our patients had their hip fractures surgically fixed within the recommended time frame. Our management approach lacked the multidisciplinary integration that is recommended for these patients. Osteoporosis and frailty were largely not addressed. The results of this study served as a platform to increase awareness of osteoporosis and frailty management as part of a multidisciplinary care for fragility fractures of the hip. We have subsequently formed a multidisciplinary unit in an effort to address our treatment deficiencies and to improve these patients' outcomes.

References

1.Tp IP, Leung J, Kung AWC. Management of osteoporosis in patients hospitalized for hip fractures, Osteoporos Int(2010) **21**(4): S605-614.

2. Cassim B, Lipschitz S, Paruk F, Tipping B. Recommendations for the acute and long-term medical management of low trauma hip fractures. JEMDSA 2013;18(1):21-32.

3. Cooper C, Campion G, Melton LJ 3rd. Hip fractures in the elderly: a worldwide projection. Osteoporosis Int. 1992;2(6):285-289.

4. Robert KC, Brox WT, Jevsevar DS, Sevarino K, Management of hip fractures in the elderly. J Am Acad Orthop Surg 2015;**23**:131-137.

5. Rabenda V, Vanoverloop J, Fabri V, Mertens R. Low incidence of anti-osteoporosis treatment after a hip fracture. J Bone Joint Surg Am. 2008;**90**:2142-8.

6. Jennings LA, Andrew D, Maselli J et al. Missed opportunities for osteoporosis treatment in patients hospitalized for hip fractures. J Am Geriatr Soc. 2010;**58**(4): 650-657.

7. NIH Consensus Panel Development on osteoporosis Prevention, Diagnosis and therapy. JAMA 2001; **285**(6): 785-795.

8. Lorentzon M, Cummings SR. Osteoporosis: the evolution of a diagnosis. J Intern Med 2015;**277**: 650–661.

9. Riggs BL, Melton LJ 3rd. Evidence for two distinct syndromes of involutional osteoporosis. Am J Med 1983; **75:** 899-901.

10. Tinetti, ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. *N Engl J Med* 1988; **319:** 1701-1707.

11. Peggy MC. Gender Differences in Osteoporosis and Fractures. Clin Orthop Relat Res. 2011;**469**:1900-1905.

12. Evan Ekman F. the role of the orthopaedic surgeon in minimizing mortality and morbidity associated with fragility fractures. J Am Acad Orthop Surg 2010;**18**:278-285.

13. Pioli G. Time to surgery and rehabilitation resources affects outcomes in ortho-geriatric units. Archives of Gerontology and Geriatrics 2012;**55**: 316-322.

14. Borgbjerg FM, Schousboe B, Pedersen SJ et al, A comprehensive hip fracture program reduces complications rate and mortality, J Am Geriatr Soc 2008;**56**:1831-1838.

15. Kanchanabat B, Stapanavatr W, Meknavin S, Soorapanth C, Sumanasrethakul C, Kanchanasuttirakn P. Systematic review and meta-analysis on the rate of postoperative venous thrombo-embolism in orthopaedic surgery in Asian patients without thrombo-prophylaxis, Br J Surg 2011;**98**:1356-1364.

16. Felsenberg D, Silman AJ, Lunt M et al. Incidence of vertebral fracture in europe: results from European Prospective Osteoporosis Study(EPOS). J Bone Miner Res 2002;**17:716-24**

17. Lee HB, Mears SC, Rosenberg PB, Leoutsakos J-MS, Gottschalk A, Sieber FE. Predisposing factors for postoperative delirium after hip fracture repair in individuals with and without dementia. J Am Geriatr Soc 2011;**59**:2306-2313.

18. Lee K-H, Ha Y-C, Lee Y-K, Kang H, Koo K-H. Frequency, risk factors, and prognosis of prolonged delirium in elderly after hip fracture surgery. Clin Orthop Relat Res 2011;**469**:2612-2620.

19. Marcantonio ER, Flacker JM, Wright RJ, Resnick NM. Reducing delirium after hip fracture: a randomized trial. J Am Geriatr Soc 2001;**49**:516–522.

20. Deschodt M, Braes T, Flamaing J, Detroyer E, Broos P, Haentjens P et al. Preventing delirium in older adults with recent hip fracture through multidisciplinary geriatric consultation. J Am Geriatr Soc 2012;**60**:733–739.

21. Strotman P, Lack W, Bernstein M. Evaluation of common fractures of the hip in the elderly. Cuur Geri Rep 2016; **5**: 38-43.

22. Balach T, Paul C, Baldwin, Intravia J. Atypical Femur Fractures Associated with diphosphonate use. J Am Acad Orthop Surg 2015;**23**: 550-557.

23 Bokshan SL, DePasse JM, Daniels AH. Sarcopenia in orthopaedic surgery. Orthopedics 2016;39(2):e295-e300.

24. Unnanuntana A, Gladnick BP, Lane JM. The assessment of fracture risk. J Bone Joint Surg Am.2010;**92**(3):743-753.

25. Reyes C, Hitz M, Alhambra DP, Risks and benefits of Bisphosphonates therapies, J. Cell. Biochem 2016 ;**117**: 20-28.

26.Keneth W, Cathleen S, Jay S, Jonatha D, Carl F, Carlos M. Zolendronic Acid and Clinical fractures and Mortality after Hip Fracture. N Engl J Med 2007;**357**: 1799-809.

27. Deting X, Fangcai L, Gang C, ShiguiY, Zhijun P. Do bisphosphonates affect bone healing? A meta-analysis of randomized controlled trials. Journal of orthopaedic surgery and research 2014;**9**: 1-45.

28. Morley P, Whitefield JF, Willick GE, parathyroid hormone; An anabolic treatment for osteoporosis. Curr pharm Des 2001;**7**(8)671-87.

29. Cummings SR, San Martin J, McClung MR, Siris ES, Eastell R, Reid IR, et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. N Engl J Med 2009;**361**(8):756-65.

30. Atteritano M, Catalano A, Santoro D, Lasco A, Benvenga S. Effects of Strontium Ranelate on markers of cardiovascular risk in postmenopausal osteoporotic women. Endocrine 2016;**53**(1):305-312.

31.Boonen S, Rosenberg E, Claessens F, Vander schueren D, Papapoulos S. Inhibition of cathepsin K for treatment of osteoporosis. Curr Osteoporos Rep.2012 Mar;**10**(1):73-9.

32. Kaufman JD, Bolander ME, Bunta AD, et al. Barriers and solutions to osteoporosis care in patients with a hip fracture. J Bone Joint Surg Am 2003;85:1837-42.

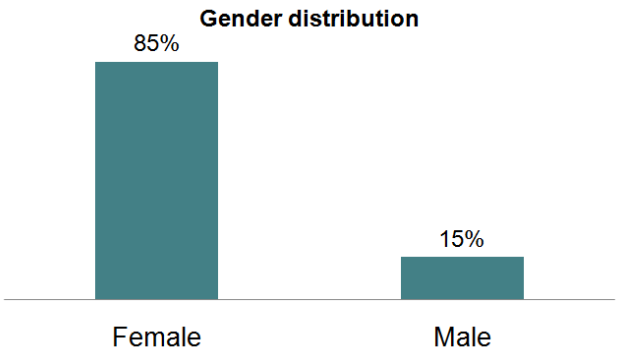

Fig 1 Gender Distribution.

85% of patients were female and 15% were males.

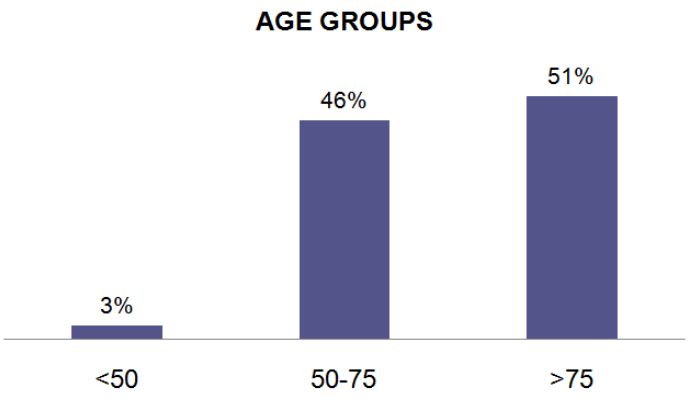

Fig 2 Age distribution. The majority of patients were older than 75 years of age

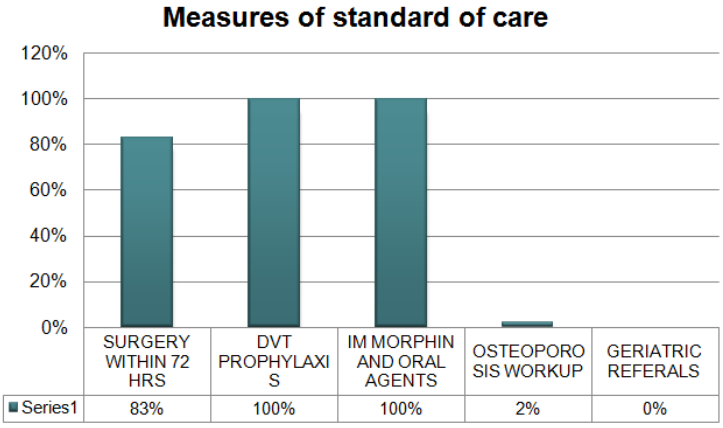

Fig 3 Measures of standard of care: only 2% of patients investigated for osteoporosis and no geriatric referrals

PART D - APPENDICES

I. ACKNOWLEDGEMENTS

1. Dr N KAUTA : MMED student, co-investigator and primary author
2. DR S Maqungo: Principal investigator, supervisor and editor of final script.
3. Other authors listed on the manuscript provided technical advices on the study design.

II. ETHICS APPROVAL

Please see attached letter from the Department of Humain research committee.

UNIVERSITY OF CAPE TOWN

Faculty of Health Sciences
Human Research Ethics Committee

Room E52-Z4 Old Main Building

Groote Schuur Hospital

Telephone [021] 406 6338 • facsimile [021] 406 6411

Email: shuretta.Thomas@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

17 June 2015

HREC REF: 325/2015

Dr S Maqungo
Orthopaedic Surgery
H49, OMB

Dear Dr Maqungo

PROJECT TITLE: MANAGEMENT OF HIP FRAGILITY FRACTURES AT GROOTE SCHUUR HOSPITAL, QUALITY ASSESSMENT PROJECT (Dr N Kauta)

Thank you for your response to the Faculty of Health Sciences Human Research Ethics Committee received on 11 June 2015.

It is a pleasure to inform you that the HREC has formally approved the above-mentioned study.

Approval is granted for one year until the 30th of June 2016.

Please submit a progress form, using the standardized Annual Report Form If the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.

(Forms can be found on our website: www.health.uct.ac.za/fhs/researCh/humanethics/forms)

Please quote the HREC REF in all your correspondence.

We acknowledge that the MMED student, Dr Ntambue Kauta will be also involved in this study.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal Investigator.

Yours sincerely

Signature removed

PROFESSOR M BLOCKMAN
CH RS , EARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki guidelines.

The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/ 135/95) and FDA Code Federal Regulation Part 50, 56 and 312.